UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TAKEDA PHARMACEUTICAL CO, LIMITED, et al. Plaintiff, v. ZYDUS PHARMACEUTICALS USA INC., et al. Defendant.	Civil Action No. 10-1723 (JAP) **OPINION** FILED UNDER TEMPORARY SEAL

PISANO, District Judge.

This is an action for patent infringement brought by Plaintiffs Takeda Pharmaceutical Company Limited, Takeda Pharmaceuticals North America, Inc., Takeda Pharmaceuticals LLC, and Takeda Pharmaceuticals America, Inc. (collectively "Takeda" or "Plaintiffs") against Zydus Pharmaceuticals (USA) Inc. ("Zydus") and Cadila Healthcare Limited ("Cadila") (collectively or "Defendants") pursuant to the Hatch-Waxman Act, 21 U.S.C. § 355(j). Plaintiffs bring this action in response to the filing by Zydus of an abbreviated new drug application with the U.S. Food and Drug Administration ("FDA") seeking approval to market and sell a generic version of Plaintiffs' drug product, Prevacid SoluTab. A four-day bench trial was held from March 26 to April 1, 2013, and this Opinion constitutes the Court's findings of fact and conclusions of law. After careful consideration of the record before it, the Court finds in favor of Plaintiffs.

I. BACKGROUND

A. The Parties[1]

Plaintiff Takeda Pharmaceutical Company Limited ("Takeda Japan") is a Japanese corporation, having a principal place of business at 1-1, Doshomachi 4-chome, Chuoku, Osaka, Japan. Amended Complaint (D.I.[2] 98) ¶ 1. Takeda Japan is involved in the research, development, and marketing of pharmaceutical products. *Id.*

Plaintiff Takeda Pharmaceuticals North America, Inc. ("TPNA") is a Delaware corporation, having a principal place of business at One Takeda Parkway, Deerfield, Illinois 60015. *Id.* ¶ 2. As part of its business, TPNA is involved in the research, development, and marketing of pharmaceutical products. TPNA has the exclusive right to import lansoprazole orally disintegrating tablets and to sell them to Takeda Pharmaceuticals LLC. *Id.*

Plaintiff Takeda Pharmaceuticals LLC ("Takeda LLC") is a Delaware limited liability company, having a principal place of business at One Takeda Parkway, Deerfield, Illinois 60015. *Id.* ¶3. Takeda LLC is involved in the purchase and sale of pharmaceutical products. Takeda LLC is the exclusive licensee of the patent-in-suit, U.S. Patent No. 6,328,994 ("the '994 Patent"). *Id.*

Plaintiff Takeda Pharmaceuticals America, Inc. ("Takeda America") is a Delaware corporation, having a principal place of business at One Takeda Parkway, Deerfield, Illinois 60015. *Id.* ¶ 4. Takeda America is involved in the purchase, sale and marketing of pharmaceutical products. Takeda America has the exclusive right to sell lansoprazole orally-disintegrating tablets to the public under the patents. *Id.*

[1] Ethypharm, S.A., a named plaintiff, sought relief in this action solely with respect to U.S. Patent No. 5,464,632. All claims relating to this patent were resolved, however, prior to trial.
[2] To reference entries on the Court's docket, the abbreviation "D.I." (docket index) is used.

Defendant Zydus Pharmaceuticals USA Inc. ("Zydus") is a pharmaceutical company primarily engaged in the sale of generic pharmaceutical products. Amended Complaint ¶ 6.

Defendant Cadila Healthcare Limited ("Cadila") is a pharmaceutical company primarily engaged in the business of researching, developing, and manufacturing pharmaceutical products. Amended Complaint ¶ 7.[3]

B. The ANDA Filing

On or about February 19, 2010, Zydus sent a letter to Plaintiffs (the "Notice Letter") informing Plaintiffs that Zydus had filed abbreviated new drug application ("ANDA") No. 200816 with the FDA seeking approval to market and sell a generic version of Plaintiffs' Prevacid SoluTab ("Prevacid") product in 15 mg and 30 mg strengths. Amended Complaint, at ¶ 32; Answer, at ¶ 32. The Notice Letter included a Paragraph IV statement pursuant to 21 USC § 355(j)(2)(b) whereby Zydus informed Plaintiffs that, in Zydus's opinion, the Orange Book patents covering Prevacid were invalid and/or would not be infringed by Zydus's commercialization of the product described in its ANDA. Amended Complaint, at ¶ 32; Answer, at ¶ 32. This action followed.

C. The Patent-In-Suit

Originally, there were four patents at issue in this action: United States Patent Nos. 6,328,994 (the "'994 patent"), 7,431,942 (the "'942 patent"), 7,875,292 (the " '292 patent") and 5,464,632 (the " '632 patent"). The '632 patent expired on November 7, 2012. By agreement, the parties withdrew all claims and counterclaims related to the '632 patent, the '942 patent and the '292 patent prior to the commencement of trial. D.I. 327. Plaintiffs' also withdrew any claims of infringement of claim 2 of the '994 patent. Trial Transcript ("Tr.")

[3] Although named as a defendant in this action, Plaintiffs presented no evidence at trial regarding Cadila with respect to any of the allegations brought against Cadila in the complaint.

7:15-23. Thus, only claim 1 of the '994 patent remained at issue in this case at the start of trial.

The '994 patent is directed to lansoprazole orally disintegratable tablets. As stated above, Plaintiffs allege that Defendants infringe claim 1 of the '994 patent. Specifically, Plaintiffs contend that Defendants infringe the claim limitation of claim 1 related to the average particle diameter of fine granules in the claimed invention.

D. Witnesses At Trial

In its infringement case-in-chief, Takeda called Dr. Brian Fennerty and Dr. David E. Bugay. Dr. Bugay was proffered as an "expert in pharmaceutical formulation" and testified regarding infringement. Tr. 75:1-4; DTX 23. Dr. Fennerty, a Board certified gastroenterologist, was not proffered as an expert, and he testified about proton pump inhibitors ("PPIs"), Prevacid SoluTab, and orally disintegrating tablets ("ODTs"). See Tr. 44:19-22, 53:13-15, 55:14 to 56:4; DTX 22. Takeda also called Adam Zaeske, Vice President of Managed Markets and Trade for Takeda America and formerly the senior director of marketing for the gastrointestinal franchise for TPNA.[4] Mr. Zaeske's testimony was directed toward the harm that would be suffered by Takeda if Zydus were to launch their ANDA product.

Defendants proffered Dr. Harry Brittain as an expert witness in the areas of physical chemistry and the science of formulation. Tr. 256:24 to 257. Defendants also called Dr. Paula Meyer-Stout, an Associate Professor of Pharmaceutics at the University of West Virginia, Tr. at 430:21-431:3; DTX 17, who was proffered and accepted as an expert in the areas of pharmaceutical chemistry and industrial pharmacy. Tr. 433:6-10.

[4] Due to scheduling issues and with consent of Defendants, Plaintiffs called Mr. Zaeske out of order.

In rebuttal to Defendants' invalidity claims, Plaintiffs called Dr. Stephen Byrn, who was proffered and accepted as an expert in physical chemistry and the science of formulation. Tr. 477:6-9, DTX 25.

The parties also submitted the deposition testimony of a number of fact witnesses who were unavailable for trial.

E. Credibility Determinations

With respect to the witnesses appearing live at trial, the Court had the opportunity to hear their testimony and observe their demeanor. Having done so, the Court has made certain credibility determinations as well as determinations relating to the appropriate weight to accord various testimony. Such determinations are reflected the factual findings set forth in Opinion.

II. FINDINGS OF FACT AND CONCLUSIONS OF LAW

The Court has heard all witness testimony and considered the documentary evidence, and, as stated above, has accorded weight to the evidence as deemed appropriate. The parties having submitted their proposed findings of facts and conclusions of law, the Court finds that a preponderance of the evidence submitted supports the facts proposed by Plaintiffs.

A. The '994 Patent

The '994 patent is directed toward novel ODT formulations containing fine granules of enteric-coated acid-labile drug. *See* DTX 2 at Abstract. According to the patent specification, the fine granules in the novel ODT formulations have an average particle diameter of about 400 μm or less. DTX 2 at col. 5, ll. 57-63. The '994 patent also addresses difficulties in producing ODTs that contain an acid-labile active ingredient (*i.e.*, lansoprazole); acid-labile ingredients are susceptible to degradation in acidic environments.

Because the drug will degrade in the acidic environment of the stomach, formulations with an acid-labile active ingredient must be designed so that the active ingredient is not released as it passes through the stomach, but rather is released in the intestine. Tr. 55:3-13. The '994 patent teaches using an enteric-coated drug granule to achieve this result. DTX 2 at col. 2, ll. 25-30.

It is possible that tablet compaction may cause problems for enteric-coated drug granules. The pressure of the compression can cause the enteric coat to crack. Without an intact enteric coat, the drug can escape from the granule and release in the mouth, esophagus or stomach, instead of the intestine, making the drug susceptible to degradation or inactivation. Tr. 54:20 to 55:13. To overcome the issue of damage to the enteric coat, the '994 patent teaches an enteric coat made from a combination of enteric-coating agent and sustained-release agent; this combination cushions the granules during tablet compression and prevents cracking of the enteric coat, thereby increasing acid-resistance of the formulation. DTX 2 at col. 2 l. 56 to col. 3, l. 3; col. 9, ll. 9-26; col. 19, ll. 25-31; *see also* Tr. 524:18 to 526:4. The '994 patent discloses an "acid resistance" test (*see* DTX 2, col. 19, ll. 25- 31), which is a "test for the integrity of the granules." Tr. at 526:5-24.

A stated objective of the invention of the '994 patent is good mouth feel, that is, an OTD containing fine granules that do not cause roughness in the mouth. Notably, however, good mouth feel/absence of roughness in the mouth is not a limitation in claim 1 of the '994 patent.

Claim 1 of the '994 patent is as follows:

> 1. An orally disintegrable tablet which comprises (i) fine granules having an average particle diameter of 400 m or less, which fine granules comprise a composition coated by an enteric coating layer comprising a first component

> which is an enteric coating agent and a second component which is a sustained-release agent, said composition having 10 weight % or more of an acid-labile physiologically active substrate that is lansoprazole and (ii) an additive wherein said tablet having a hardness strength of about 1 to about 20 kg, is orally disintegrable.

'994 Patent claim 1, DTX 2; Tr. at 7:24 to 8:7.

B. Person of Ordinary Skill in the Art

The scope and analysis of the '994 patent is to be undertaken by the hypothetical "person of ordinary skill in the art" or "POSA." Defendants' expert, Dr. Meyer-Stout, defined a person of ordinary skill in the art at the time of the filing of the application leading to the '994 Patent as someone with a high level of education (such as a Ph.D. in Pharmaceutical Chemistry or Pharmaceutics), and several years of training or experience devoted to the study of drug formulation and manufacturing, dosage form disintegration, multiparticulate systems and particle size analysis. Tr. at 443:17 to 444:10. Plaintiffs' expert, Dr. Byrn testified that a person of skill in the art at the relevant time would have a lower level of skill, specifically, someone with a college degree in chemistry, pharmaceutical sciences, pharmacy or chemical engineering with at least four years of industry experience. Nevertheless, for the purposes of his testimony at trial, Dr. Byrn assumed that the hypothetical person of skill in the art was the person defined by Dr. Meyer-Stout. As the testimony of Defendants' witness, Dr. Meyer-Stout, and Plaintiffs witness, Dr. Byrn, assumed the same person of skill in the art, the Court need not resolve the dispute between Dr. Byrn's definition and Dr. Meyer-Stout's, and shall accept Dr. Meyer-Stout's definition for the purposes of this analysis.

C. Infringement

1. Burden of Proof and Legal Standards

Plaintiffs have the burden of proving that Defendants infringed the '437 patent by a preponderance of the evidence. *Carroll Touch Inc. v. Electro Mechanical Systems, Inc.*, 15 F.3d 1573, 1578 (Fed. Cir. 1993). It is an act of infringement to submit an application under § 505(j) of the Federal Food, Drug, and Cosmetic Act (*i.e.*, 21 U.S.C. § 355(j)) for a drug claimed in a patent or the use of which is claimed in a patent, if the purpose of such submission is to obtain approval to engage in the commercial manufacture, use, or sale of that same drug before the expiration of such patent. *See* 35 U.S.C. § 271(e)(2)(A); *see also Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1346 (Fed. Cir. 2000) ("[M]ere act of filing an ANDA constitutes infringement."). The question under 35 U.S.C. § 271(e) (2)(A) is whether the drug that is the subject of the ANDA will infringe the patent when approved and marketed. *See Bristol–Myers Squibb Co. v. Royce Labs., Inc.*, 69 F.3d 1130, 1135 (Fed. Cir. 1995). Thus, to meet its preponderance of the evidence burden, the patentee must show that it is more likely than not that the proposed ANDA product would, if commercially marketed, meet the claim limitations of the patent-in-suit. *See Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1287 (Fed. Cir. 2010); *Warner–Lambert Co. v. Teva Pharms. USA, Inc.*, 418 F.3d 1326, 1341 n.15 (Fed. Cir. 2005).

The infringement analysis proceeds in two steps -- the first is proper construction of the relevant claims, and the second is a comparison of those claims to the accused product or method. *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1288 (Fed. Cir. 2009). To prove infringement, the patentee must show that an accused product or method is within the claim limitations of the patent-in-suit either literally or under the doctrine of equivalents. *See*

Amgen, 580 F.3d at 1374; *Warner Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21, 117 S.Ct. 1040, 137 L.Ed.2d 146 (1997). "A patent is infringed if any claim is infringed ... for each claim is a separate statement of the patented invention." *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1220 (Fed. Cir. 1995). Infringement, whether literal or under the doctrine of equivalents, is a question of fact. *Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1353 (Fed. Cir. 1998).

a. Literal Infringement

Literal infringement exists if any one of a patent's asserted claims covers the alleged infringer's product or process. *See Markman v. Westview Instr.*, 517 U.S. 370, 374, 116 S.Ct. 1384, 134 L.Ed.2d 577 (1996). Literal infringement is shown where each limitation of at least one asserted claim of the patent-in-suit is found in the alleged infringer's product or process. *See Hormone Research Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558, 1562 (Fed. Cir.1990); *Panduit Corp. v. Dennison Mfg. Co., Inc.*, 836 F.2d 1329, 1330 n.1 (Fed. Cir. 1987). Proof of literal infringement may be based on direct or circumstantial evidence. *See Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1372 (Fed.Cir.2009) ("A patentee may prove infringement by any method of analysis that is probative of the fact of infringement ... and circumstantial evidence may be sufficient ....") (citations and internal quotes omitted).

b. Direct Infringement

A person is liable for direct infringement if he "without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefore." 35 U.S.C. § 271(a). Direct infringement requires a party to perform each and every step or element of a claimed method or product." *BMC Res., Inc. v. Paymentech, L.P.*, 498 F.3d 1373, 1378 (Fed. Cir.

2007). "If any claim limitation is absent from the accused device, there is no literal infringement as a matter of law." *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1247 (Fed. Cir. 2000).

2. Claim Construction

The Court held a *Markman* hearing on May 26, 2011, and subsequently issued its claim construction Opinion. *See* D.I. 113. The Court construed the claim term "fine granules having an average particle diameter of 400 μm or less" to mean "fine granules up to and including the enteric coating layer having an average particle diameter of 400 μm (±10%) or less." D.I. 113 at 7. The evidence at trial showed that a POSA would understand the Court's construction "400 μm (±10%) or less" to mean "440 μm or less." The "+" 10% creates an upper threshold of 440 μm or less (mathematically, 10% of 400 μm is 40 μm; 400 μm plus 40 μm is 440 μm). Tr. at 80:25 to 81:2. A POSA would find the minus 10% immaterial because the minus 10%-- which yields 360 μm or less -- is already encompassed by the 440 μm or less range. Tr. 3/26/13 at 81:3-14 ("because 360 microns is encompassed by the upper threshold of 440 microns, we only pay attention to the 440 micron value"); Tr. 3/28/13 at 480:12-24 ("when you read the patent, you go from 440 and 360 becomes redundant"). Under the Court's construction, the upper limit of the "fine granules" within claim 1 as 440 μm.

In its claim construction Opinion, the Court did not construe the claim term "average particle diameter" finding that there was "no ambiguity with [the] phrase and its ordinary and customary meaning would be clear to one skilled in the art." *See* D.I. 113 at 5.

3. Infringement Analysis

Zydus conceded at trial that its ANDA product would meet all the limitations of claim 1 of the '994 patent but one. D.I. 315 at §2; Tr. at 79:16-21. Zydus disputed that its ANDA

product contains "fine granules having an average particle diameter of 400 µm or less," as that term has been construed by the Court. D.I. 315 at §2; Tr. at 79:16-21. Consequently, a focus of the infringement portion of the trial was the parties' disagreement as to whether individual coated granules in Zydus's ANDA product that are stuck together (referred to as agglomerates) should be deagglomerated into their component, individual coated entities and counted as separate granules for purposes of determining average particle diameter of Zydus's "fine granules." Takeda argued that agglomerates should be deagglomerated into their component, individual parts when determining the average particle diameter of the "fine granules" in claim 1 of the '994 patent. Tr. at 13:25 to 14:6. Zydus, on the other hand, argued that individual granules that become stuck together as agglomerates should be counted as a single particle when determining average particle diameter of the "fine granules" in claim 1 of the '994 patent. Tr. at 15:7-10.

a. A POSA's Understanding of "Fine Granules"

The '994 patent specification and claim 1 of the '994 patent describe "fine granules" as individual, coated granules. DTX 2 at col. 15, l. 26 to col. 16, l. 27, Claim 1. The '994 patent specification describes a "fine granule" as comprising a single "core" that is as uniform a sphere as possible. DTX 2 at col. 15, ll. 33-35; *see also* Tr. at 81:15 to 82:2. This core is coated with a drug layer and then an enteric coating layer to obtain a "fine granule being in the form of a rough sphere." DTX 2 at col. 15, l. 26 to col. 16, l. 27; *see also* Tr. at 81:15 to 82:9. The patent defines "spherical" to include forms with a "curved surface" such as "eggplants and drops." DTX 2 at col. 5, ll. 40-42. But the '994 patent uses "spherical" to describe the shape of the "core," the basic building block of the "fine granule." *See* DTX 2 at

col. 14, l. 40 to col. 15, l. 26. Nowhere does the '994 patent teach that a "fine granule" can be built from more than one spherical core.

Claim 1 is consistent with the teachings of the '994 patent specification. Claim 1 teaches an ODT that includes "fine granules." These "fine granules comprise a composition...having 10 weight % or more of...lansoprazole." DTX 2 at col. 37, ll. 44-51; *see also* Tr. at 82:10-19. That drug composition is, in turn, "coated by an enteric coated layer." *Id.* The "fine granules" of claim 1 refer to individual enteric-coated granules that contain the drug lansoprazole. *Id.*

As Dr. Bugay testified, agglomerates are undesired in the pharmaceutical manufacturing industry; unlike individual coated granules, agglomerates "may not perform in a consistent manner" so that the patient gets "the consistency of the administration of the active [drug] in that tablet." Tr. at 104:4-8, 245:23 to 246:6. Both Plaintiffs' and Defendants' experts agree that the goal of pharmaceutical manufacturing is to generate individual coated granules, not agglomerates. Tr. at 103:13 to 104:3 (Dr. Bugay, Takeda's expert, testifying that the "aim is to produce individual particles, individual granules"); Tr. at 156:18-21; Tr. at 266:16-17 (Dr. Brittain, Defendants' expert, testifying that "ideally what you would like to make are individual particles that receive the coating"). It is the objective of pharmaceutical manufacturing to optimize the process such that one achieves individual coated granules. Tr. at 103:13 to 104:3; 245:20 to 246:16.

Based upon the evidence at trial, the Court concludes that in the context of the '994 patent, a POSA knows to deagglomerate prior to subjecting the sample to particle size measurement; it is the goal of particle size determination to measure individual or primary particles. Tr. at 205:13-21; 105:13-14; 244:15-24. Indeed, the user manual of the HELOS

RODOS – which is the laser diffraction instrument disclosed in the '994 patent as an exemplary particle size measurement instrument (DTX 2 at col. 5, ll. 43-50) – explicitly instructs users that "it needs to be ensured that the sample is free of agglomerates" (emphasis added). *See* PTX 84 at 3.

b. Measuring "Average Particle Diameter"

The '994 patent defines "average particle diameter" to mean "volume based median diameter (median diameter: 50% particle diameter from cumulative distribution), unless otherwise specified." See DTX 2, col. 5, ll. 43-46. The median diameter is commonly known as "d50." Tr. at 92:15-17. The volume based median diameter is referred to as "volume-based d50." Tr. at 92:7-17. Median diameter refers to the value where "50 percent of the particles are above that micron size and 50 percent of the particles are below that micron size." Tr. at 97:24 to 98:2. A POSA would understand that volume-based d50 is a proper measurement of "average particle diameter" in relation to the '994 patent. Tr. at 268:7-21. The parties agree that the "average particle diameter" of claim 1 references "volume based distribution median particle diameter," or d50 for short, as no other measure of average particle diameter is specified. See Tr. at 92:7-17; 267:25 to 269:20.

Although the '994 patent identifies laser diffraction as an example of a method to determine "average particle diameter," that determination is not limited to measurement by that method. *See* DTX 2, col. 5, ll. 46-47 (average particle diameter "can be measured by, for example, a laser diffraction particle distribution measurement method"). As noted earlier, the '994 patent identifies HELOS RODOS as an exemplary laser diffraction instrument. A POSA would understand that other standard measurement methods, such as optical microscopy, can be used to measure average particle diameter. Both parties' experts agree that optical

microscopy is a standard technique for measuring average particle diameter. Tr. at 93:1-2 (Dr. Bugay, Takeda's expert, testifying that optical microscopy is a "standard technique"); Tr. at 338:3-6 (Dr. Brittain, Zydus's expert, agreeing that optical microscopy is a "standard technique").

c. Zydus's ANDA Product

Zydus's ANDA product comes in a 15mg and 30 mg "dosage strength[]." PTX 42 at 1, 13-14; *see also* Tr. at 78:12-15. The product contains fine granules which Zydus refers to in its documents as pellets. PTX 42 at 12; *see also* Tr. at 76:8-17. These pellets "deliver lansoprazole to the patient." Tr. at 76:18-20. Zydus utilizes "the same common pellets" for both 15 mg and 30 mg strengths. PTX 131 at Z0155977 and PTX 132 at Z0156088; *see also* Tr. at 78:22 to 79-10. Thus, the 30 mg strength of the ANDA product is a direct scaleup of the 15 mg strength. Tr. at 78:22 to 79-10.

Zydus's ANDA includes a color-coded depiction that Zydus calls a "[s]chematic representation of enteric coated pellets" for its ANDA product. PTX 42 at 12. This schematic shows that ANDA product's pellets comprise a core coated by the drug layer containing lansoprazole. *See* Tr. at 76:21 to 77:2; see PTX 42 at 12. The drug layer is coated with a barrier coating layer followed by the enteric coating layer. Tr. at 77:3- 14; see PTX 42 at 12. The enteric coating layer protects the lansoprazole in the drug coating layer from the acidic pH of the stomach. Tr. at 77:8-14; *see* PTX 42 at 12. The enteric coating layer is coated by a finishing coating layer. Tr. at 77:15-17; see PTX 42 at 12. The purpose of the finishing coating layer is to "protect[] breakage of the pellets during compression." Tr. at 78:2-11; *see also* PTX 42 at 29.

Both parties' experts describe the granules in Zydus's ANDA product as generally spherical in shape. Dr. Bugay, Takeda's expert, testified that Zydus's pellets are "spheroidal in shape" and "generally spherical." Tr. at 88:7-10; *see also* Tr. at 119:5-6. Dr. Brittain, Zydus's expert, testified that the granules in Zydus's ANDA product are "irregularly-shaped spheres." Tr. at 341:18-20.

The individual coated pellets in Zydus's ANDA product are the "fine granules" of the '994 patent. *See* PTX 42 at 12; *see also* Tr. at 82:20 to 83:14. Dr. Bugay, Takeda's expert, testified that there is a "direct correlation" between Zydus's pellet and the elements of claim 1 of the '994 patent. *Id.*; PTX 42 at 12; PTX 1, Claim 1. In determining the average particle diameter of the "fine granules" of the '994 patent, it is these individual coated pellets that should be subjected to particle size analysis.

[redacted]

d. Agglomerates - Zydus ANDA Product

The vast majority of granules in Zydus's ANDA product are individual granules. A 30 mg Zydus ANDA tablet contains approximately 6,000 individual coated granules. Tr. at 85:19-22; PTX 217. Over 80% of the granules are individual granules. Tr. at 120:20-24; see

also PTX 217. Approximately 18% of the granules are made up of two "fine granules" stuck together, about 1.5% of the granules are made up of three "fine granules" stuck together, and far less than 1% of the granules are three or more "fine granules" stuck together. Tr. at 121:6-12, 121;19-24; *see also* PTX 217.

Dr. Bugay confirmed via Raman spectroscopy that agglomerates in Zydus's ANDA product were comprised of component, individual enteric-coated entities. Tr. at 107:2-7, 108:19 to 110:17; PTX 216; PTX 219. Raman spectroscopy is a "chemical identification technique" that produces an image identifying a compound and where that compound is located in the sample. Tr. at 107:8 to 108:2. Raman spectroscopy showed that, for example, an agglomerate made of two individual pellets in Zydus's ANDA product comprises "two different layers of lansoprazole that are associated with these two granules that are agglomerated together." Tr. at 109:11-19; PTX 216; PTX 219. These "two individual granules [were] adhered together because of the enteric coat." Tr. at 110:8-13; PTX 216; PTX 219. "Zydus's schematic [representation of enteric coated pellets in its ANDA product] corresponds to" the Raman image. Tr. at 110:14-17.

e. Fine Granules in Zydus's ANDA Product

Zydus produced to Takeda 15 mg and 30 mg strength tablets of Zydus's ANDA product. Tr. at 83:16-21; see also PTX 129. The 15 mg strength was from exhibit batch EMM320 and the 30 mg strength was from exhibit batch EMM321. Tr. at 83:22-24; *see also* PTX 129. Both EMM321 and EMM320 were manufactured in March 2012 and completed in June 2012. See PTX 131 at Z0155975; PTX 132 at Z0156086. The EMM320 and EMM321 exhibit batches incorporated pellets from the same exhibit batch EMM227 of "common pellets". PTX 132 at Z0156087 (identifies EMM227 as the batch for the "common pellets"

for the EMM321 batch); PTX 131 at Z0155976 (identifies EMM227 as the batch for the "common pellets" for the EMM320 batch); PTX 133 (batch manufacturing record of the EMM227 "common pellets"). EMM227 was manufactured in March 2012 and completed in May 2012. PTX 133 at Z0155623.

Takeda's expert, Dr. Bugay performed particle size tests on three 30 mg strength tablets of Zydus's ANDA product from the EMM321 batch. Tr. 83:25 to 84:1, 84:25 to 85:1; PTX 130. He tested 100% of the granules contained within each tablet, a total of over 18,000 granules. Tr. 85:2-12, 23-25; PTX 217. According to Dr. Bugay, an "objective of any pharmaceutical manufacturing process is to produce a consistent product from batch-to-batch, tablet-to-tablet." *Id.* His testing was based on a representative sample of Zydus's ANDA tablets. Tr. at 85:2-12, 85:23-25.

Zydus's EMM320 exhibit batch contained 15 mg strength tablets of Zydus's ANDA. The 15 mg strength tablets of Zydus's ANDA product contained the same pellets – *i.e.*, pellets from Zydus's EMM227 exhibit batch – as Zydus's 30 mg strength tablet. See PTX 132 at Z0155976; see also PTX 132 at Z0156087. The 30 mg strength is a direct scale-up of the 15 mg strength. Tr. at 78:22 to 79:10; PTX 131 at Z0155977 and PTX 132 at Z0156088. Because the 30 mg and 15 mg strength tablets use the same common pellets, it was sufficient for Dr. Bugay to test only the 30 mg strength tablets to determine whether the "fine granules" in Zydus's 15 mg and 30 mg ANDA product meet the contested limitation of Claim 1 of the '994 patent. Tr. at 83:25 to 84:6, 117:13-21. There appears to be no dispute that testing of granules from the 30 mg tablet provides comparable results to testing of granules from the 15 mg tablet.

Claim 1 is directed to "fine granules" taken from a compressed tablet. Tr. at 367:12-19 (Zydus's expert testifying that claim 1 is directed to "fine granules within a tablet" and confirming that Dr. Bugay tested the granules within the tablet); 457:18 to 458:5 (Dr. Meyer-Stout opining that the average particle diameter "must refer to the particle size population in the compressed finished tablet" and confirming that Dr. Bugay measured the granules extracted from the compressed finished tablet). To extract the enteric-coated pellets in Zydus's ANDA product, Dr. Bugay used what he described as a "very simple extraction procedure" using an "aqueous buffer solution of pH 4.5." Tr. at 86:22 to 87:15. A washing solution with a pH of 4.5 was selected because the enteric coating layer of Zydus's pellets dissolve at a pH of 5.5 and above. Tr. at 87:16-22. Dr. Bugay chose a washing solution with a pH that was well below the pH required to solubilize the enteric coating layer of Zydus's ANDA pellets. *See id.* That extraction procedure is well known to a POSA. Tr. at 87:23 to 88:1. Dr. Bugay washed each tablet and decanted the filtrate (liquid portion) from the extracted pellets three times. Tr. at 87:3-15.

Dr. Bugay's extraction process freed the pellets from the tablet and removed the finishing coating layer. Tr. at 91:3-16; PTX 42 at 12. That extraction process resulted in enteric-coated pellets that were subjected to particle size analysis. Tr. at 91:3-16; PTX 42 at 12. Dr. Bugay tested the filtrate for the presence of lansoprazole with a high performance liquid chromatography ("HPLC") instrument. Tr. at 88:11-14. Dr. Bugay detected less than 1% lansoprazole in the filtrate for each ANDA tablet that he tested, which demonstrated that Dr. Bugay's extraction process "did not adversely affect the integrity of the enteric coat of the Zydus pellets." Tr. at 88:20-24, 90:20-22; PTX 220. He "did not see any cracking" of the enteric coat. Tr. at 119:11-12. Dr. Bugay used Raman spectroscopy to show that the enteric

coat remained intact after his extraction procedure. Tr. at 110:19 to 111:1, 119:14-21; PTX 214. To the extent that Zydus argues that the extraction procedure could have affected particle size of the "fine granules," the Court finds no evidence of this and notes that Zydus's expert admitted that he did "not perform[] any studies regarding whether extraction of the granules by Dr. Bugay impacted the particle size of Zydus's granules." Tr. at 362:10-17. Additionally, Zydus's own documents reflect that it measured particles extracted from its tablets with no indication of cracking or other degradation. See PTX 70 at 1, 3; Tr. 531:22 - 533:6; Kharkar Dep. Tr. at 116:5-16.

f. Measuring Particles in Zydus's ANDA Product

As noted above, the '994 patent does not limit particle size measurements to any particular method, and the parties' experts agree that optical microscopy is a standard technique to measure average particle diameter. *See* Tr. at 93:1-2; 338:3-6. Both parties' experts acknowledge that laser diffraction and optical microscopy are both "widely recognized," standard techniques that indirectly measure volume- based d50 of irregularly-shaped particles. Tr. at 100:1-9 (testimony of Dr. Bugay, Takeda's expert, stating the similarities of laser diffraction and optical microscopy); Tr. at 338:3-6, 341:15-20, 343:3-14 (testimony of Dr. Brittain, Zydus's expert stating the similarities of laser diffraction and optical microscopy). However, laser diffraction has one limitation that optical microscopy does not have. It is known in the art that laser diffraction "cannot distinguish between...single particles and...clusters of primary particles forming an agglomerate or an aggregate." DTX 64 at 2314, PTX 16 at 1; Tr. at 104:22 to 105:4. "If the presence of aggregates is suspected," the U.S. Pharmacopeia ("USP") – which is a standard setting body – directs POSAs to "other

techniques such as microscopy," when measuring particle size. *See* DTX 64 at 2314, PTX 16 at 1; Tr. at 106:10-17; Trial Tr. 3/28/13 at 486:21-22.

Because "fine granules" in the '994 patent are individual coated entities, if the sample contains more than nominal agglomerates, then optical microscopy is proper; laser diffraction is appropriate if the sample contains individual fine granules with nominal agglomeration. Tr. at 105:25 to 106:9. Consequently, due to laser diffraction's known limitation, laser diffraction is inadequate to measure the volume-based d50 of the "fine granules" in Zydus's ANDA product because about 20% of the granules in Zydus's ANDA product are agglomerates. Tr. at 121:6-12, 121:19-24; PTX 217.

To determine the average particle diameter of the "fine granules" in Zydus's ANDA product, Takeda's expert Dr. Bugay measured volume-based d50 consistent with the teachings of the '994 patent. Tr. 92:18-22; *see also* PTX 1 at col. 5, ll. 43-46. Dr. Bugay used optical microscopy to determine the volume-based d50 of the "fine granules" in Zydus's ANDA product. To obtain the volume-based d50 of the "fine granules" in Zydus's ANDA product, Dr. Bugay used the standard deagglomeration feature included in the image analysis software accompanying his CILAS optical microscope. *See* PTX 19 at 17; Tr. at 111:14 to 113:12.

For the three samples, Dr. Bugay obtained a volume-based d50 of 413.76 µm, 426.94 µm, and 416.24 µm. Tr. at 114:9-13; PTX 217; PTX 218. He averaged these volume-based d50s to determine an average particle diameter of 418.98 µm for the "fine granules" in Zydus's ANDA product. Tr. at 114:3-8; PTX 217; PTX 218. However, due to the presence of less than 1% lansoprazole in the filtrate, Dr. Bugay adjusted the volume-based d50 upward to 420.46 µm. Tr. at 115:24 to 116:19; PTX 217; PTX 218. Thus, the highest possible

volume-based d50 of the "fine granules" in Zydus's ANDA product is 420.46 µm and is still below the upper limit of claim 1 of the '94 patent – 440 µm. Tr. at 117:6-11, 117:22 to 118:4, 137:25 to 138:5. Consequently, Zydus's ANDA product infringes claim 1 of the '994 patent.

[redacted] The Court disagrees.

[redacted] *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241 (Fed. Cir. 2000) ("*Elan*") [redacted] Tr. at 26:14-25. *Elan* involved a patent of Bayer's claiming a drug containing nifedipine crystals of a specific surface area ("SSA") – 1.0 to 4.0 m2/g. *Elan*, 212 F.3d at 1246. Elan amended its ANDA to specify that its drug product would only contain nifedipine crystals with a SSA of 5 m2/g or greater. Along with its ANDA, Elan filed a certificate of analysis ("COA") performed by an independent laboratory, which stated the measured SSA of the nifedipine crystals used in Elan's drug product was 6.15 m2/g. Further, Elan's nifedipine supplier was prohibited from selling in the United States nifedipine with a SSA under 4.7 m2/g. Also, at FDA's request, Elan defined its method of testing to ensure the nifedipine's SSA [size] to be 5 m2/g or greater: Elan would measure the SSA of its nifedipine no more than five business days before tablet manufacture and would discard any nifedipine having a SSA of less than 5 m5/g.

In *Elan*, the plaintiff Bayer did not contend, nor did it offer any evidence, that Elan's drug would literally infringe its patent. Instead, Bayer speculated that the SSA of the nifedipine crystals would reduce over time to a measurement that fell within the claimed SSA size. Finding Bayer's speculation did not raise an issue of fact, the court granted Elan's motion for summary judgment. *Elan*, 212 F.3d at 1254. The Federal Circuit affirmed, agreeing that Elan's ANDA specification "defines its product in a way that directly addresses the question of infringement – the SSA [size] of nifedipine crystals." *Id.* at 1249-50.

[redacted] Plaintiffs point to *Bayer AG v. Biovail Corp*, 279 F.3d 1340 (Fed. Cir. 2002) ("*Biovail*"), a subsequent case filed by the same plaintiff on the same patent. Based on the first case, Elan argued that Bayer was collaterally estopped from litigating infringement. *Elan* had involved an ANDA for a 30 mg drug product. *Biovail* concerned the same patent at issue in *Elan* and a "nearly identical" ANDA for a 60 mg version of the same drug product. The Federal Circuit held that the "nearly identical" ANDA in the second action did not directly resolve the issue of infringement, and ordered the district court to consider evidence outside the ANDA. *See Bayer AG v. Biovail Corp.*, 279 F.3d 1340, 1346-47 (Fed. Cir. 2002). The factual evidence differed in the Biovail because the plaintiff had done actual testing of Elan's ANDA product. Consequently, evidence derived from the testing of Elan's commercial product created a genuine dispute as to whether Elan's ANDA defined the compound with sufficient particularity to answer the infringement inquiry. *Id.* at 1346-47.

In the instant case, the Court finds, contrary to Defendants' contentions, *Elan* to be inapplicable in light of the testing performed by Plaintiffs' expert on product Zydus intends to commercialize. This testing has shown that the EMM batch contains fine granules with an

average particle diameter less than 440 microns and, therefore, infringes claim 1 of the '994 patent.

[redacted] Tr. at 132:13-23. [redacted] Tr. at 131:5-8. [redacted] PTX 21 at Z0155906; PTX 22 at Z0155924; PTX 23 at Z0155948-49. As stated earlier, laser diffraction does not differentiate between individual granules and agglomerates. Tr. 129:12-20; 302:15 to 303:2, 314:2-13; DTX 64 at 2314; PTX 16 at 1. Defendants' counsel at trial conceded that if the Court were to determine that the '994 patent requires deagglomeration to measure particle size properly (and the Court has so found), [redacted] and Elan would not be not applicable. Tr. 622:17 to 623:24.

[redacted]. Tr. at 132:13-23; 336:6-13 (Zydus uses static sampling). Zydus relies on static sampling to collect enteric coated granules prior to subjecting those granules to particle size testing. Tr. at 335:10 to 336:13. However, Zydus's expert, Dr. Brittain, admits that static sampling does not obtain a representative sample; only dynamic sampling can yield the desired representative sample. Tr. 360:12-24 (agreeing that "only sampling from a bulk powder while it is in motion can yield the desired representative sample").

Given the above, this case is more akin to the circumstances in *Biovail*. Here, Takeda has done actual testing and has evidence that the ANDA product that Zydus intends to commercialize does infringe the Takeda patent such that there is a "genuine disput[e] as to whether the ANDA specification defines the compound with sufficient particularity to answer the infringement inquiry." *See Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). [redacted]. PTX 26 at Zydus-Supp000001; Gurram Dep. Tr. at 56:15-17; 56:19-20. However, when Plaintiffs' expert tested the "fine granules" in the EMM batch, the average particle diameter of those "fine granules" in the EMM batch was less than 440 μm and thus, infringe claim 1 of the '994 patent.

In sum, the Court finds [redacted] that Zydus's ANDA product infringes the '994 patent.

D. Invalidity

1. Burden of Proof

Every claim of an issued patent is independently presumed valid. *See* 35 U.S.C. § 282. Consequently, a party challenging the validity of a patent claim must prove invalidity by clear and convincing evidence, and although the burden of production may switch to the patentee, the burden of proof always remains with the challenger. *See id.*; *Microsoft Corp. v. i4i Ltd. Partnership*, --U.S. --, 131 S.Ct. 2238, 2243, 180 L.Ed.2d 131 (2011); *Innovative Scuba Concepts, Inc. v. Feder Indus., Inc.*, 26 F.3d 1112, 1115 (Fed. Cir. 1994). Clear and convincing evidence is a higher burden of proof than preponderance of the evidence. *See Colorado v. New Mexico*, 467 U.S. 310, 316, 104 S.Ct. 2433, 81 L.Ed.2d 247 (1984). It is

evidence that places in the mind of the finder of fact an abiding conviction that the truth of the factual contentions is highly probable. *See id.* Clear and convincing evidence should "instantly tilt[ ] the evidentiary scales" in favor of its proponent when weighed against the opposing evidence.

2. Written Description and Enablement

One of the statutory conditions for patentability under the Patent Act is adequate disclosure of the invention. As set forth in Section 112 of Title 35,

> [t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112. The Federal Circuit has interpreted § 112 as imposing a number of separate disclosure requirements, two of which are relevant here. The first is known as the written description requirement, found in the first sentence of Section 112, which requires that the specification contain an adequate "written description of the invention." 35 U.S.C. § 112; *see also Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1353-54 (Fed. Cir. 2010) (en banc) ("[A] separate requirement to describe one's invention is basic to patent law. Every patent must describe an invention. It is part of the *quid pro quo* of a patent; one describes an invention, and, if the law's other requirements are met, one obtains a patent. The specification must then, of course, describe how to make and use the invention (*i.e.*, enable it), but that is a different task.").

"[T]he purpose of the written description requirement is to 'ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification.'" *Ariad Pharms., Inc. v.*

Eli Lilly & Co., 598 F.3d 1336, 1353-54 (Fed.Cir.2010) (en banc). It "serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based and to demonstrate that the patentee was in possession of the invention that is claimed." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005).

As stated by the Federal Circuit, "[t]he test for sufficiency of a written description is whether the disclosure clearly allow[s] persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Crown Packaging Technology, Inc. v. Ball Metal Beverage Container Corp.*, 635 F.3d 1373, 1380 (Fed. Cir. 2011) (internal quotations omitted, alterations in original). The "hallmark of written description is disclosure," and a court examining the sufficiency of a written description must make "an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Ariad*, 598 F.3d at 1351. To pass muster under that inquiry, "[t]he disclosure must reasonably convey[ ] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Crown*, 635 F.3d at 1380 (internal quotations omitted, alteration in original). Said another way, "the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Ariad*, 598 F.3d at 1351.

"[D]etermining whether a patent complies with the written description requirement will necessarily vary depending on the context." *Id.* The requirement "must be applied in the context of the particular invention and the state of the knowledge." *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005). The inquiry into the written description requirement is a question of fact." *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1361 (Fed. Cir. 2011) (quoting *PowerOasis, Inc. v. T–Mobile USA, Inc.*, 522 F.3d 1299, 1307 (Fed. Cir.

2008)). A party challenging a patent based upon the written description requirement must provide clear and convincing evidence that persons skilled in the art would not recognize in the disclosure a description of the claimed invention. *Centocor Ortho Biotech, Inc. v. Abbott Laboratories*, 636 F.3d 1341, 1347 (Fed. Cir. 2011) (presumption of validity overcome only by clear and convincing evidence).

Separate from the written description requirement is the "enablement" requirement codified in § 112. "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *ALZA Corp. v. Andrx Pharmaceuticals, LLC*, 603 F.3d 935, 940 (Fed. Cir. 2010) (quoting *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). "Enablement is not precluded where a 'reasonable' amount of routine experimentation is required to practice a claimed invention, however, such experimentation must not be 'undue.'" *Id.* In *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988), the Federal Circuit set forth the following factors that a court may consider when determining if a disclosure requires undue experimentation:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

858 F.2d at 737. A court need not consider all of the *Wands* factors in its analysis, but rather, a court is only required to consider those factors relevant to the facts of the case. *See Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991).

Importantly, to fulfill the enablement requirement, the full scope of each claim must be enabled. *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008).

> Enabling the full scope of each claim is part of the *quid pro quo* of the patent bargain. A patentee who chooses broad claim language must make sure the broad claims are fully enabled. The scope of the claims must be less than or equal to the scope of the enablement to ensure that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims.

Id. It is not sufficient for the specification to provide merely "a starting point, a direction for further research"; it must provide "reasonable detail" sufficient to enable a person of ordinary skill in the art to make or use the invention. *Automotive Technologies Intern., Inc. v. BMW of North America, Inc.*, 501 F.3d 1274, 1284 (Fed. Cir. 2007). Whether the enablement requirement has been satisfied is a question of law based upon underlying facts, and is determined as of the patent's effective filing date. *Sitrick*, 516 F.3d at 999.

a. Particle Size Measurement

As noted above, the '994 patent is not limited to particle size measurements conducted by laser diffraction. PTX 1, at col.5, ll. 46-47. The '994 patent specification identifies laser diffraction as an example of a particle size measurement method: "[Average particle diameter] can be measured by, for example, a laser diffraction particle distribution measurement method." *Id.* The Court has recognized that its claim construction of the term "fine granules having an average particle diameter of 400 μm or less" was not limited to particle size measurements by laser diffraction. *See* D.I. 317 at 5 ("Defendants now assert that the Court's claim constructions that incorporate the ±10% deviation apply only to laser diffraction . . . . However, the Court did not construe the above mentioned terms to include any such limitations."). Zydus' expert, Dr. Meyer-Stout, testified that a POSA could turn to methods apart from laser diffraction to measure average particle diameter. See Trial Tr. 3/28/13 at 434:3-11 ("Q. In addition to laser diffraction . . . what methodologies might be available to the

ordinary artisan to determine average particle diameter for granular distribution in the 300 micron to 450 micron size? A. Well, I would consider several methods. Possibly you could use analytical sieving, microscopy, you could use light obscuration methods and you would consider Coulter counter methods.").

Defendants contend that claim 1 of the '994 patent is invalid under 35 U.S.C. §112 for lack of enablement because they allege that there are certain methodologies for the determination of average particle diameter which cannot be utilized without undue experimentation. Specifically, Defendants contend that a POSA would not know what Coulter counter instrument parameters and sample preparation techniques to apply when measuring the particle size of fine granules. Tr. at 631:14 to 632:2. Dr. Meyer-Stout asserted that the average particle diameter of fine granules using a Coulter counter instrument would require "a lot of experimentation" because one would need to consider choosing an adequate electrolyte solution and an adequate aperture tube opening. Tr. at 448:5 to 449:11. Zydus, however, did not offer any more specific evidence of the amount of experimentation necessary to use a Coulter counter instrument or of past failed efforts to use a Coulter counter instrument to measure the average particle diameter of fine granules in an ODT of the '994 patent.

Dr. Byrn testified that "it's well within the person's skill of the art to carry out these measurements and also, the instrument companies are trying to make it turn key. They want to be able to sell their instruments so they want an instrument that's accurate but simple to use . . . . Certainly with a person as high a level as Dr. Meyer-Stout said a Ph.D. with a lot of experience, they would know how to carry out [particle size testing]." Tr. at 514:12-25. The parties do not dispute that a POSA would know how to measure particle size via laser

diffraction and/or optical microscopy. There was no evidence that a POSA would not know what laser diffraction or optical microscopy instrument parameters and sample preparation techniques to apply when measuring the particle size of fine granules. Indeed, Zydus documents showed that Zydus read the '994 patent and measured particle size using laser diffraction without undue experimentation. *See* PTX 70 at 3 ("Particle Size Distribution by Malvern," a laser diffraction instrument); PTX 81 at Z0150600 ("Method specified in patent is Laser diffraction and same method has been used for particle size"); PTX 82 at Z0152877 ("Method specified in patent is Laser diffraction and same method has been used for particle size, mahesh to confirm final particle size analysis method and its parameters"); Tr. at 515:16 to 516:12.

The Court finds that Defendants have failed to establish by clear and convincing evidence that the ‘994 patent is invalid for lack of enablement based on their allegation that there are certain methodologies for the determination of average particle diameter which could not be utilized without undue experimentation. Defendants rely primarily upon conclusory statements by it expert regarding the amount of experimentation necessary to practice the claim, and such conclusory statements do not carry Defendants’ burden. *See Pharm. Res., Inc. v. Roxane Labs. Inc.*, 253 Fed. Appx. 26, 30 (Fed. Cir. 2007).

Zydus also contends that claim 1 of the '994 patent is invalid under 35 U.S.C. §112 for lack of enablement because different particle size measurement methodologies produce different particle size results in relation to the same sample. Tr. at 40:19 to 41:2; 445:1-11. However, Zydus' theory is based on the incorrect assumption that there is only one "correct" average particle diameter for any given unknown sample that can only be measured by one particle size measurement technique. Dr. Byrn testified that a POSA would know that there is

no "single correct particle size" and that "[e]ach method is correct." Tr. at 483:17-23. Dr. Byrn concluded that a POSA would not need to engage in undue experimentation to measure the average particle diameter of fine granules. Tr. at 510:2-8 ("It's clear how to do it and it's within the skill of the art to be able to measure particle size."). Zydus's expert, Dr. Brittain, agreed with Takeda that different particle size results produced by different measurement methods are all equally correct. Tr. at 345:12-25. Dr. Brittain acknowledged that he has published a number of articles that state "the correct but differing particle size results obtained using various instruments are all equally correct, but each simply may be expressing its correct results in different terms." See Trial Tr. 3/27/13 at 345:12 to 346:17 (emphasis added). The Court, therefore, finds that Defendants have failed to show by clear and convincing evidence that claim 1 of the ‘994 patent is invalid because different particle size measurement methodologies produce different particle size results in relation to the same sample.

b. Inoperative Species

Zydus contends that the Court's claim construction of “fine granules having an average particle diameter of 400 µm or less” as incorporating a ±10% deviation renders the '994 patent invalid under 35 U.S.C. §101 and §112 for lack of enablement because it captures inoperative species – particles greater than a maximum particle size and large, conventional particles. Tr. at 40:14-18.

(i). Maximum Particle Size

The '994 patent defines the term "average particle diameter" as "volume based distribution median diameter (median diameter: 50% particle diameter from cumulative distribution), unless otherwise specified." See PTX 1 at col. 5, ll. 43-46. The '994 patent also refers to a "maximum particle size" that is "practically 425 µm or less." PTX 1 at col. 5, ll.

66-67; Tr. at 282:5 to 283:6 (Dr. Brittain testifying that the '994 patent defines "the maximum particle size" as "practically 425 microns or less"). Dr. Brittain testified that the Court's claim construction "creates trouble" because the average particle diameter limitation encompasses granules greater than 425 μm and that it is a mathematical impossibility for a median to be greater than a maximum. Tr. at 326:2 to 327:8.

However, Zydus's theory incorrectly collapses together two distinct concepts: median/average particle diameter and maximum particle diameter. The '994 patent treats the maximum particle size and the median particle diameter as two separate and distinct concepts. *See* PTX 1 at col. 5, l. 57 to col. 6, l. 3. The '994 patent first describes the median particle diameter in one paragraph and then explicitly sets that concept "aside" by stating "aside from the average particle diameter of the above 'fine granules.'" PTX 1 at col. 5, l. 57-64. The '994 patent then moves on to describe the maximum particle size in the next paragraph:

> In the present invention, "fine granules having an average particle diameter of 400 um or less, which fine granules comprise a composition coated by an enteric coating layer, said composition having 10 weight % or more of an acid-labile physiologically active substance" have an average particle diameter of about 400 μm or less, in order that roughness is not felt in the mouth. Preferably, the average particle diameter of the fine granules is 300 to 400 μm.
>
> Aside from the average particle diameter of the above "fine granules", regarding the maximum particle size, the particle diameter is practically 425 μm or less, and preferably practically 400 μm or less. Preferably, the particle diameter is practically 300 to 425 μm, more preferably 300 to 400 μm.

PTX 1 at col. 5, line 57 to col. 6, line 3.

Dr. Byrn testified that claim 1 does not include a maximum particle size limitation but that claim 7 of the '994 patent is directed to maximum particle size. Tr. at 504:5-18; PTX 1 at Claim 1, 7. Claim 7 of the '994 patent claims "[a]n orally disintegrable tablet of claim 1, wherein the particle diameter of the fine granules is practically 425 um or less," which mirrors

the specification's definition of maximum particle size. PTX 1 at claim 7; col. 5, ll. 66-67. Dr. Byrn then testified that he, a POSA, would consider claim 1 to be directed to fine granules with a median diameter of up to 440 μm, while claim 7 is a narrower subset of claim 1, only covering particles that are 425 μm or less. Tr. at 92:7-14 (Dr. Bugay testifying that average particle diameter means median diameter); Tr. at 504:19-24; PTX 1 at Claim 1, 7. If claim 1 were interpreted to include a maximum particle size limitation, claim 7 would be rendered superfluous. *See* PTX 1 at Claim 1, 7. Testimony from Zydus' expert Dr. Brittain supports this conclusion, as he testified that the '994 patent treats the median particle diameter and maximum particle diameter as "two separate and distinct definitions." See Tr. at 282:16-20, 283:9-14.

(ii). Conventional Granules

The '994 patent states, "[c]onventional granules have large particle diameters . . . . Granules having a large particle diameter (400 μm or more of average particle diameter) also produce a feeling of roughness in the mouth." PTX 1 at col. 2, ll. 12-18. Zydus contends that the Court's claim construction would read upon inoperative, conventional granules associated with a bad mouth feel. Tr. at 40:14-18. Dr. Brittain testified that the "Background Art" section of the '994 patent defined conventional granules as having a hard cut off of 400 μm or more. Tr. at 286:25 to 288:5. However, the '994 patent distinguishes the "fine granules" and "conventional granules" concepts. *Compare* PTX 1 at col. 2, ll. 12-18 (stating conventional granules produce a feeling of roughness in the mouth) with PTX 1 at col. 5, ll. 57-63 (stating that fine granules do not produce a feeling of roughness in the mouth). The '994 patent describes "fine granules" as having "an average particle diameter of about 400 μm or less in order that roughness is not felt in the mouth." *See* PTX 1 at col. 5, ll. 57-63. Consistent with

the Court's claim construction, Dr. Byrn testified that a POSA would understand the language "about 400 µm or less " to incorporate a 10% variation and that the patent associates granules of 440 µm or less with a good feeling in the mouth. Tr. at 506:7-25. Thus, a POSA would understand that conventional granules, defined as producing a rough feeling in the mouth, to be 440 µm or greater. Tr. at 507:6-23.

As the Federal Circuit has noted, "[e]ven if some of the claimed combinations were inoperative, the claims are not necessarily invalid. 'It is not a function of the claims to specifically exclude . . . possible inoperative substances . . . .'" *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984) (citation omitted); *Warner Lambert Co. v. Teva Pharms. USA, Inc.*, Civ. No. 99-922 (DRD), 2007 WL 4233015, at *14 (D.N.J. Nov. 29, 2007). "Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid." *Atlas*, 750 F.2d at 1576- 1577; *Pharm. Res.*, 253 Fed. App'x at 30; *see also Warner*, 2007 WL 4233015 at *14 (finding "no evidence in this case that the number of inoperative combinations is so significant as to force one of ordinary skill in the art to experiment unduly in order to practice the claimed invention."). Here, the Court finds that Zydus has not met its burden of proving, by clear and convincing evidence, that claim 1 of the '994 patent is invalid for lack of enablement for capturing inoperative species -- large, conventional particles and particles greater than a maximum particle size.

c. Granules Post-Tableting

Zydus contends that claim 1 of the '994 patent is invalid under 35 U.S.C. § 112 for lack of written description and lack of enablement (a) because the '994 patent does not teach

how to extract granules from a finished tablet for particle size measurement and (b) because the average particle diameter of the granules pre-tableting and post-tableting may not be the same due to the compression forces during tableting. Tr. at 41:3-8; 453:18-22, 455:3-5, 453:23 to 454:13.

(i). Extraction

Dr. Meyer-Stout testified that the '994 patent specification only discloses measurement of pre-tableted granules and does not teach measurement of post-tableted granules (*i.e.*, how to extract granules from a finished tablet for particle size measurement). Tr. at 453:18-22, 455:3-5. It is undisputed that claim 1 of the '994 patent is directed to post-tableted granules. *See* Tr. at 367:12-15; 457:23 to 458:2. Dr. Meyer-Stout and Dr. Brittain both testified that the average particle diameter limitation of claim 1 refers to fine granules within a compressed, finished tablet." Tr. at 367:12-15 ("[Q.] Now, it's your position, isn't it, that the claims of the '994 patent are directed to the fine granules within a tablet. Is that correct? A. Yes, I believe that's exactly what the claim says."); Tr. at 457:18 to 458:2 (Dr. Meyer-Stout agreeing that her expert report states, "The average particle diameter limitation of the claims must refer to the particle size population in the compressed finished tablet"). Defendants offered no evidence that a POSA would not know how to extract granules from a finished tablet prior to subjecting those granules to particle size testing. Defendants also offered no evidence as to how much experimentation would be necessary for a POSA to extract granules from a finished tablet.

According to Takeda's expert, Dr. Byrn, no special training or education is required of a POSA to extract fine granules from a compressed tablet for particle size testing. Tr. at 530:24 to 531:3 ("a technician could do the extraction quite easily"). Indeed, the entire point of an ODT is to allow for easy extraction of granules in a person's mouth. Tr. at 531:12-16

("if it didn't do that, it wouldn't work like an ODT. . . when a person takes an ODT, they're really doing an extraction themselves"). Dr. Bugay measured granules that were extracted from a compressed, finished tablet prior to conducting his particle size analysis. Tr. at 367:17-19; 458:3-5.

It appears based on Zydus's own testing of the particle size of granules during development of its ANDA product that Zydus had no difficulty extracting granules from finished tablets to measure for particle size; there is no evidence of undue experimentation by Zydus. *See* PTX 70 at 1, 3. In an internal e-mail dated March 31, 2009, Zydus indicated that it measured the particle size of "pellets separated from pilot batch tablets," "pellets separated from exhibit batch tablets," and "pellets separated from scaleup batch tablets." *See* PTX 70 at 1, 3; Tr. at 531:22-533:2. Zydus' Rule 30(b)(6) witness, Srinivas Gurram, also confirmed this fact. *See* Gurram Dep. Tr. 127:7-12, 128:4-8 ("[Q.] Is it fair to say that Zydus performed particle size testing on pellets that were extracted from its lansoprazole ODT tablets by Malvern laser diffraction and microscopy? A. Yes, that form of testing, yes."). Zydus' employee in its Intellectual Property Department, Pallavi Kharkar, further testified that Zydus employees were able to measure particle size of granules after they were removed from Zydus' proposed ANDA product. *See* Kharkar Dep. Tr. at 116:5-16 ("Q. So they were able to figure out a way to measure particle sizes after tablet compression? A. I think so.").

Dr. Byrn testified that he did not see any indication in any Zydus documents that Zydus had difficulty extracting granules from tablets prior to subjecting those granules to particle size determination. *See* Trial Tr. 3/28/13 at 533:3-6.

(ii). Compression

Dr. Meyer-Stout also contended the '994 patent is invalid under 35 U.S.C. §112 for lack of written description and lack of enablement because the average particle diameter of the granules pre-tableting and post-tableting may not be the same due to the compression forces during tableting. Tr. at 453:23 to 454:13. Claim 1 of the '994 patent is directed to an ODT with a hardness range of "about 1 to about 20 kg." *See* PTX 1, at Claim 1. Dr. Meyer-Stout asserted that the claimed hardness range corresponds to the amount of compression forces used during tableting; she testified that, the harder the tablet, the more impact compression forces would have on granules in the tablet. Tr. at 451:7 to 452:6 ("as I go to a harder tablet, that those forces would have even more of an impact on the granules in the tablet"). However, Zydus offered no test results evidencing that compression forces would impact particle size. Dr. Meyer-Stout admitted that she did not perform any testing assessing the impact of compression on the particle size of the granules in Zydus' ANDA product. Tr. at 456:21-24 ("I did not perform any tests, yes."). In fact, Dr. Meyer-Stout testified that she could not predict the impact compression forces allowed under the '994 patent would have on the granules:

> Q. What effect would an increase or decrease in hardness strength have on the D(0.50) post-tabletting versus pre-tabletting?
>
> A. Well, if what you're asking, well, post-tabletting, I couldn't predict, for example, the change in the D(0.50) relative to the D(0.50) pre-tabletting. That's just because of all that's going on in the physics of compression. We do fracture some particles, but then they may also fuse to other particles, so I couldn't predict the direction that would go, but in general, one would anticipate in these ranges that as you go up to these higher hardnesses, you would anticipate you may get then an increase in your D(0.50).
>
> Q. Could you also get a decrease in your D(0.50)?

A. That's possible.

Tr. at 454:14 to 455:2.

Zydus also offered no evidence as to how much experimentation is required for a POSA to determine the impact of compression on particle size. In contrast, Dr. Byrn and Dr. Bugay testified that compression forces would not impact the average particle diameter of the fine granules in Zydus' ANDA product. Tr. at 524:1-13; *see also* 118:23 to 119:2 ("[Q.] [L]et's talk about factors that could have impacted your determination of average particle size. What impact did compression forces during tabletting have? A. In my opinion, none."). In fact, Zydus ANDA product contains a finishing coat; the purpose of the finishing coating layer is to "protect breakage of the pellets during compression." *See* PTX 42 at 29; Tr. at 78:2-11. Dr. Bugay also examined the granules first-hand to confirm that the enteric-coated granules were still spherical in shape and thus, compression did not significantly deform the granules. Tr. at 119:3-10.

Dr. Byrn noted that the '994 patent specifically teaches "an orally disintegrable preparation . . . having suitable strength (hardness) so that it will not be damaged through production processes or handling." *See* PTX 1, at col. 2, line 56 to col. 3, line 3; Tr. at 524:18 to 525:6. The '994 patent teaches the inclusion of an enteric coat and sustained release agent in order to cushion the granules during tablet compression and prevent cracking of the enteric coat. PTX 1, at col. 9, lines 9-26; Tr. at 525:19 to 526:4. The '994 patent also discloses an acid resistance test, that is aimed at testing whether the integrity of the enteric-coated granules is damaged during compression. *See* PTX 1, at col. 19, lines 25-31; Tr. at 526:5-22.

Dr. Byrn further testified that compression forces during tableting of an ODT are not so high as to affect the average particle diameter of the granules in an ODT. Tr. at 524:1-13

("We have to remember, ODTs need to dissolve in the mouth. You're giving them to children and people that can't chew very well and so they have to break apart in the mouth. So you can't put [ODTs] under high compression forces that might affect the granules. It's just not common sense."). Dr. Byrn disagreed with Dr. Meyer-Stout's contention that a 20 kg tablet would be "very, very hard" because "it wouldn't be an ODT if it was very, very hard . . . it wouldn't dissolve in the mouth." Tr. at 451:21-22, 528:24 to 529:4. In any event, Dr. Bugay tested Zydus' ANDA product to have a hardness of 3.2 to 3.4 kp. Tr. at 559:2-7.

(iii). *Eli Lilly*

Zydus relies on *Eli Lilly & Co. v. Teva Pharms. USA, Inc.*, 619 F.3d 1329, 1344 (Fed. Cir. 2010), in support of its contention that the '994 patent is invalid for lack of written description. In *Eli Lilly*, the patent-at-issue claimed drug particles of a specified particle size range. *See* 619 F.3d at 1344. Teva had altered its particle size manufacturing specification of its bulk drug to a non-infringing size. Nevertheless, Eli Lilly's expert tested the particle size of the drug particles in Teva's finished ANDA tablet and determined that, even though the drug particles were not infringing pre-tableting, the drug particles extracted from the finished tablet fell within the claimed size range. The district court construed Eli Lilly's patent as including both pretableted drug particles and post-tableted drug particles. The district court also noted that the patent did not disclose how to extract drug particles from a tablet, nor did the inventors perform any tests to determine how the granulation or the tableting process could affect particle size. The district court then determined that a POSA would not know how to extract particles from a finished tablet for purposes of particle size measurement "so as to make it unnecessary for the inventors to specify the procedure for doing so." *Eli Lilly & Co. v. Teva Pharms. USA*, Inc., 657 F. Supp. 2d 967, 1027 (S.D. Ind. 2009).

Additionally, the district court found that without measuring the drug particle size extracted from a finished tablet, a POSA would not know whether the drug particles were infringing because a POSA would not know whether the drug particle subjected to granulation or tableting would "increase in particle size, decrease, or stay the same." *See id.* at 1027 n.56. Thus, the district court held that Eli Lilly's patent was invalid for lack of written description. *See id.* at 1028.

The Federal Circuit affirmed the district court, noting the district court's finding that a POSA would not know how to extract the drug particles from a finished tablet for particle size measurement and further noting that Eli Lilly's own expert conceded that "[o]ne reading the [Particle Size Patent] in 1996 would not know whether the particle size was being increased or decreased [or remain the same] in the formulation." *See Eli Lilly*, 619 F.3d at 1344-1345 (citation omitted).

Eli Lilly is inapposite. The district court in *Eli Lilly* concluded that a POSA would not know how to extract the particles from a finished tablet for particle size testing. See Eli Lilly, 657 F. Supp. 2d at 1027. Here, a POSA would know how to extract fine granules from a finished ODT for particle size measurement; both parties' experts agreed that Dr. Bugay did precisely that – he measured the particle size of granules extracted from a finished tablet. Tr. 367:17-19; 458:3-5. Zydus' own documents, Rule 30(b)(6) witness, and Intellectual Property Department employee further admitted that Zydus, itself, has successfully extracted granules from a finished tablet for particle size measurement without difficulty. PTX 70, at 1,3; Tr. 127:7-12; 128:4-8; 116:5-16.

Furthermore, in *Eli Lilly*, the district court only considered the impact of compression forces on particle size in the context where a POSA would not know how to extract drug

particles from a finished tablet. *See Eli Lilly*, 657 F. Supp. 2d at 1027 n.56. In contrast, here, a POSA would know how to extract fine granules from an ODT.

The Court finds that Defendants have not met their burden of proving, by clear and convincing evidence, that claim 1 of the '994 patent is invalid for lack of enablement or written description based on allegations that the specification does not teach how to measure post-tableted granules and because the average particle diameter of the granules pre-tableting and post-tableting may not be the same because of compression forces during tableting.

2. Indefiniteness

To be sufficiently definite, a patent specification must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, ¶ 2. The boundaries of the claim must be discernible to one skilled in the art based on the language of the claim, the specification, and the prosecution history, as well as that person's knowledge of the relevant field of art. *See Halliburton Energy Servs., Inc. v. M–ILLC*, 514 F.3d 1244, 1249–51 (Fed. Cir. 2008). Claims that are "not amenable to construction" or "insolubly ambiguous" are indefinite. *Datamize LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir. 2005). The Federal Circuit has noted that "because claim construction frequently poses difficult questions over which reasonable minds may disagree, proof of indefiniteness must meet an exacting standard." *Haemonetics Corp. v. Baxter Healthcare Corp.*, 607 F.3d 776, 783 (Fed. Cir. 2010) (quotations omitted). "[A] claim is indefinite only if the 'claim is insolubly ambiguous, and no narrowing construction can properly be adopted.' " *Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1338–39 (Fed. Cir. 2003) (*quoting Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001).). However, "[i]f the meaning of the

claim is discernible, even though the task may be formidable and the conclusion may be one over which reasonable persons will disagree, we have held the claim sufficiently clear to avoid invalidity on indefiniteness grounds." *Exxon*, 265 F.3d at 1375.

As noted above, the Court has construed the claim term "fine granules having an average particle diameter of 400 μm or less" as incorporating a ±10% deviation. The Court also previously recognized that the '994 patent is not limited to average particle diameter determined by the laser diffraction technique. Zydus contends that the Court's claim construction renders the '994 patent invalid under 35 U.S.C. §112 for indefiniteness. Tr. at 40:9-13. Dr. Brittain testified that when the ±10% variance applied to the "400 μm or less" term, the upper limit is "somewhere between 440 and 360." Tr. at 327:9 to 328:12.

Takeda countered with expert testimony that made clear that a POSA would understand the claim term "400 μm or less ±10%" to refer to an upper limit of 440 μm or less. Tr. 508:5-23. A POSA recognizes that the "minus 10%" or "360 μm" is immaterial because it is already encompassed by the "plus 10%" or "440 μm" limit. Tr. at 81:3-14 ("because 360 microns is encompassed by the upper threshold of 440 microns, we only pay attention to the 440 micron value"); Tr. at 480:12-24 ("when you read the patent, you go from 440 and 360 becomes redundant"). The Court found both of Takeda's experts credible and gives due weight to their testimony in regard to this issue. As such, the Court finds that Defendants did not meet their burden of showing by clear and convincing evidence that the '994 patent is invalid for indefiniteness in light of the Court's construction of the claim term "fine granules having an average particle diameter of 400 μm or less," which incorporated a ±10% variance.

III. REMEDIES

The Hatch–Waxman Act explicitly authorizes several of types of relief for a prevailing patent-holder. *See* 35 U.S.C. § 271(e)(4). Included among these are orders that establish the effective date of FDA approval of the infringing drug as "a date which is not earlier than the date of the expiration of the patent which has been infringed," *id.* § 271(e)(4)(A), and, when appropriate, injunctive relief "against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug." *Id.* § 271(e)(4)(B). A plaintiff seeking a permanent injunction must demonstrate

> (1) that it has suffered an irreparable injury; (2) that remedies available at law, such as monetary damages, are inadequate to compensate for that injury; (3) that, considering the balance of hardships between the plaintiff and defendant, a remedy in equity is warranted; and (4) that the public interest would not be disserved by a permanent injunction.

eBay Inc. v. MercExchange, LLC, 547 U.S. 388 (2006). The Court finds, based on the evidence presented at trial, that Plaintiffs have demonstrated their entitlement to a permanent injunction. In particular, the Court finds that Takeda would suffer irreparable harm if Zydus is not enjoined from launching its generic version of Prevacid SoluTab until expiration of the '994 patent.

As shown at trial, the foundation of Takeda Japan's business is the research and development of innovative pharmaceutical products and the protection of those innovative products through the use of patents. Tr. at 403:7-12. The U.S. based Takeda entities – TPNA, Takeda LLC, and Takeda America – market, promote and sell the drug products developed by Takeda Japan. Tr. at 403:24 to 404:1. The revenues generated from these sales are then

funneled back to Takeda Japan to fund further research and development activities in relation to pipeline products. Tr. at 403:24 to 404:4.

Takeda's Prevacid family includes Prevacid SoluTab and the Prevacid capsules. Tr. at 405:2 to 405:10. After Prevacid capsules lost exclusivity due to expiration of the compound patent (claiming the drug lansoprazole) and generics cannibalized the vast majority of Prevacid capsules' sales and market share, revenues generated by Prevacid SoluTab became much more important for funding research and development opportunities at Takeda Japan. Tr. at 407:3-24, 408:5-10.

In October 2010, Teva launched its generic version of Prevacid SoluTab, [redacted] Tr. at 408:12-14, 410:6-12. Teva was required to withdraw its generic from the market in April 2011 due to problems with clogging nasogastric tubes and oral syringes. Tr. at 410:13-20. [redacted] Tr. at 410:21-25. Upon the withdrawal of Teva's generic [redacted] Prevacid SoluTab regained its status as the only ODT PPI available in the marketplace. Tr. at 411:7-11.

Presently, Prevacid SoluTab is the only ODT PPI available in the marketplace. Tr. at 411:7-13. As Dr. Fennerty testified, Prevacid SoluTab is especially suited for patient populations who have difficulty swallowing, such as the pediatric population. Tr. 55:14 to 56:4.

Upon entry into the market, Teva's generic immediately and significantly cannibalized the vast majority of sales and market share of Prevacid® SoluTabTM. *See* PTX 127; PTX 224; Tr. at 413:4-13.

Prior to generic entry, [redacted] *See* PTX 127; Tr. at 413:23 to 414:8. According to Mr. Zaeske testified, if no generic ever launched, he would expect Prevacid SoluTab to continue generating [redacted] consistent with its historical performance. Tr. at 417:16-22. Thus, Takeda never fully recovered from the harm caused by generic entry, even though all generics were eventually withdrawn from the market. *See* PTX 127; Tr. at 413:23 to 414:2 ("SoluTab product regained a portion of its sales but does not fully return to its historical monthly gross sales level"), 414:9-13 ("initial generic entry permanently damaged Prevacid® SoluTabTM, the brand, in terms of its revenue potential").

If Zydus were to launch its ANDA product, Takeda would suffer the same, permanent harm that it suffered as a result of Teva's generic – immediate cannibalization of market shares and sales. Tr. at 420:19 to 421:1. Similar to the impact of Teva's generic, Takeda would likely not be able to fully recover from the damage caused by entry of Zydus' generic prior to expiration of the '994 patent. Tr. 3/28/13 at 414:9-13. According to witness testimony, cannibalization of Prevacid SoluTab revenues will ultimately mean less funding for global research and development efforts by Takeda Japan. Tr. at 421:14-23. Plaintiff would be irreparably harmed in that they would lose research and development opportunities that could have been funded by Prevacid SoluTab revenues if Zydus' ANDA product is

allowed to enter the market. Tr. 421:24 to 422:5, 427:5-9 ("the value of those R&D activities is impossible to quantify") (emphasis added).

Plaintiff's evidence of harm went unrebutted, and Zydus did not offer any evidence of harm Zydus would experience if it were enjoined from launching its ANDA product. The Court finds that the relevant factors weigh in favor of enjoining Zydus from engaging in the commercial manufacture, use, offer for sale or sale within the United States, or importation into the United States, of Zydus's ANDA product until expiration of the '994 patent.

IV. CONCLUSION

As set forth above, the Court finds that Zydus infringed claim 1 of the '994 patent. The Court further finds that Defendants have not established by clear and convincing evidence that claim 1 of the '994 patent is invalid. Consequently, judgment shall be entered in favor of Plaintiffs.

/s/ Joel A. Pisano
JOEL A. PISANO, U.S.D.J.

Dated: May 7, 2013